

FIG. 1

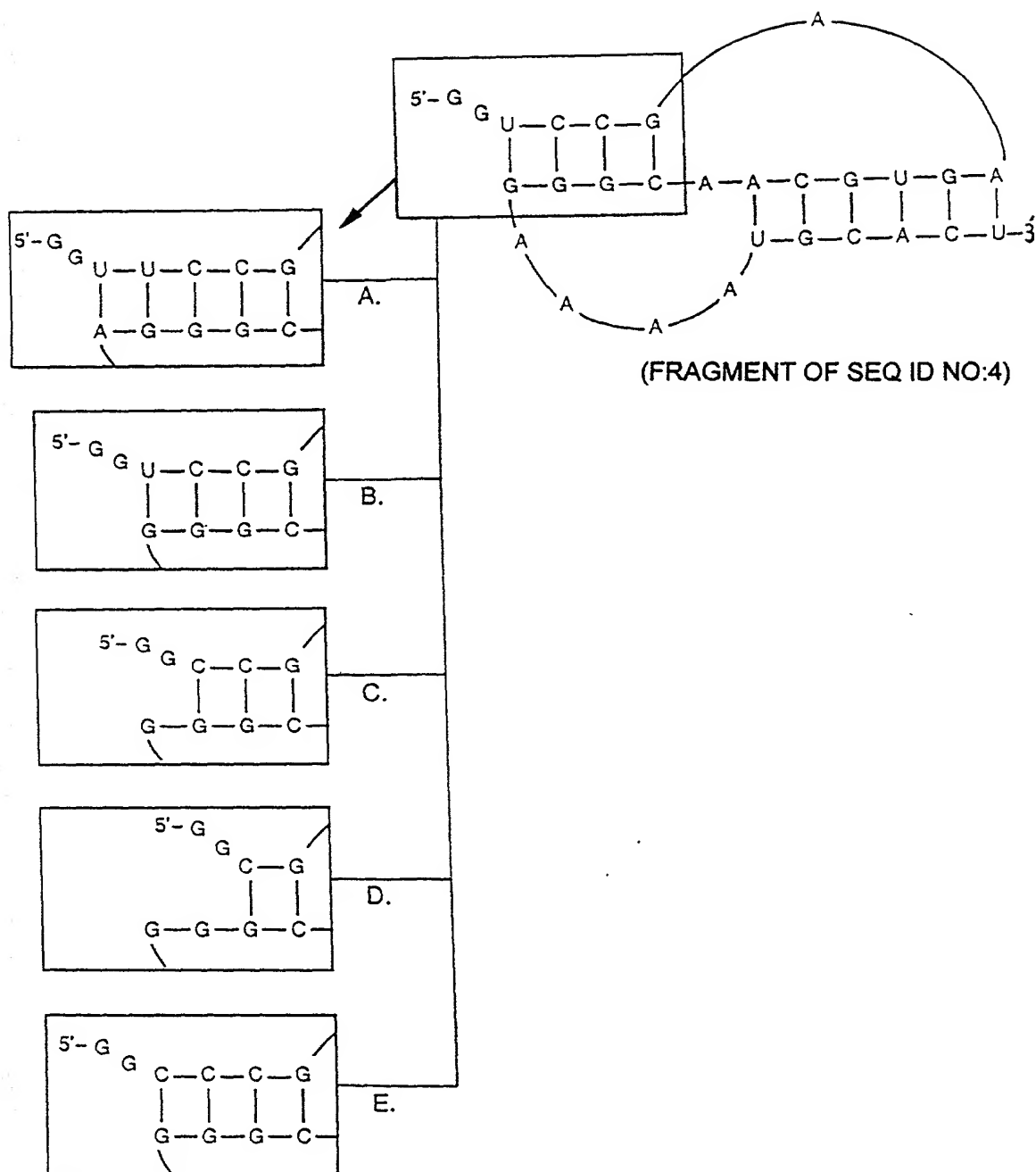


FIG. 2A

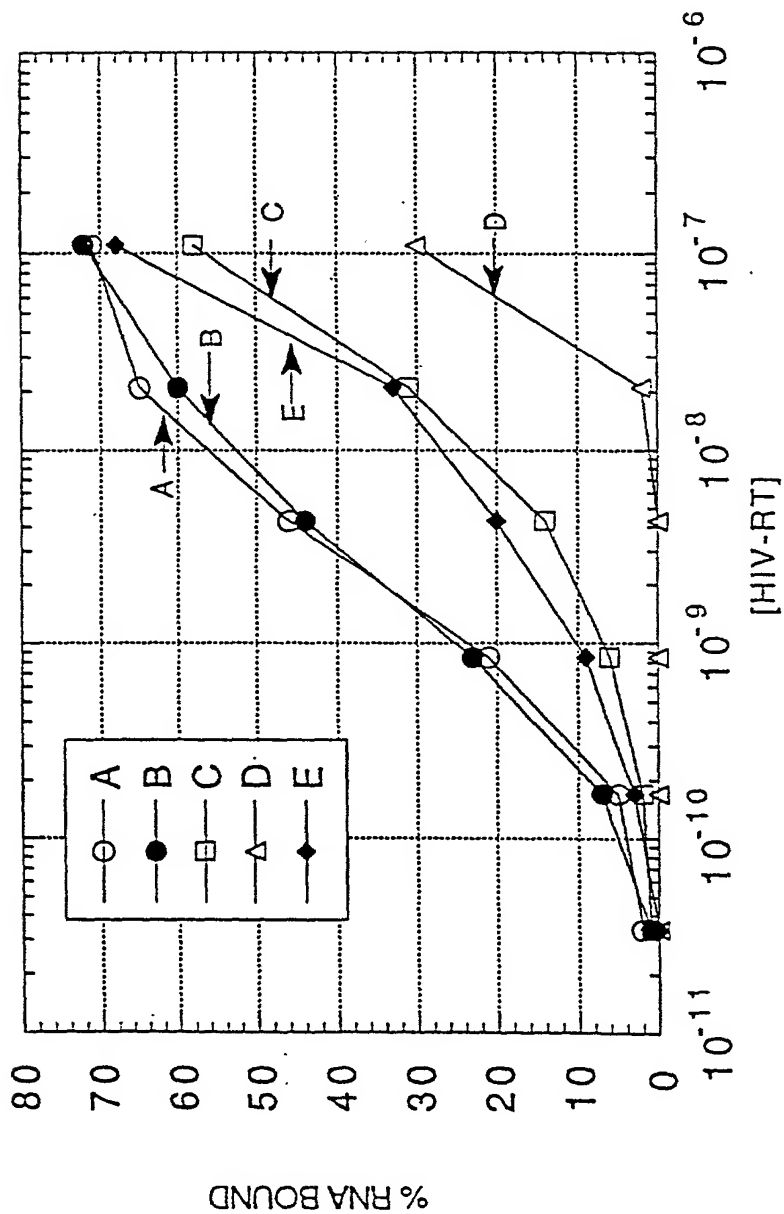


FIG.2B

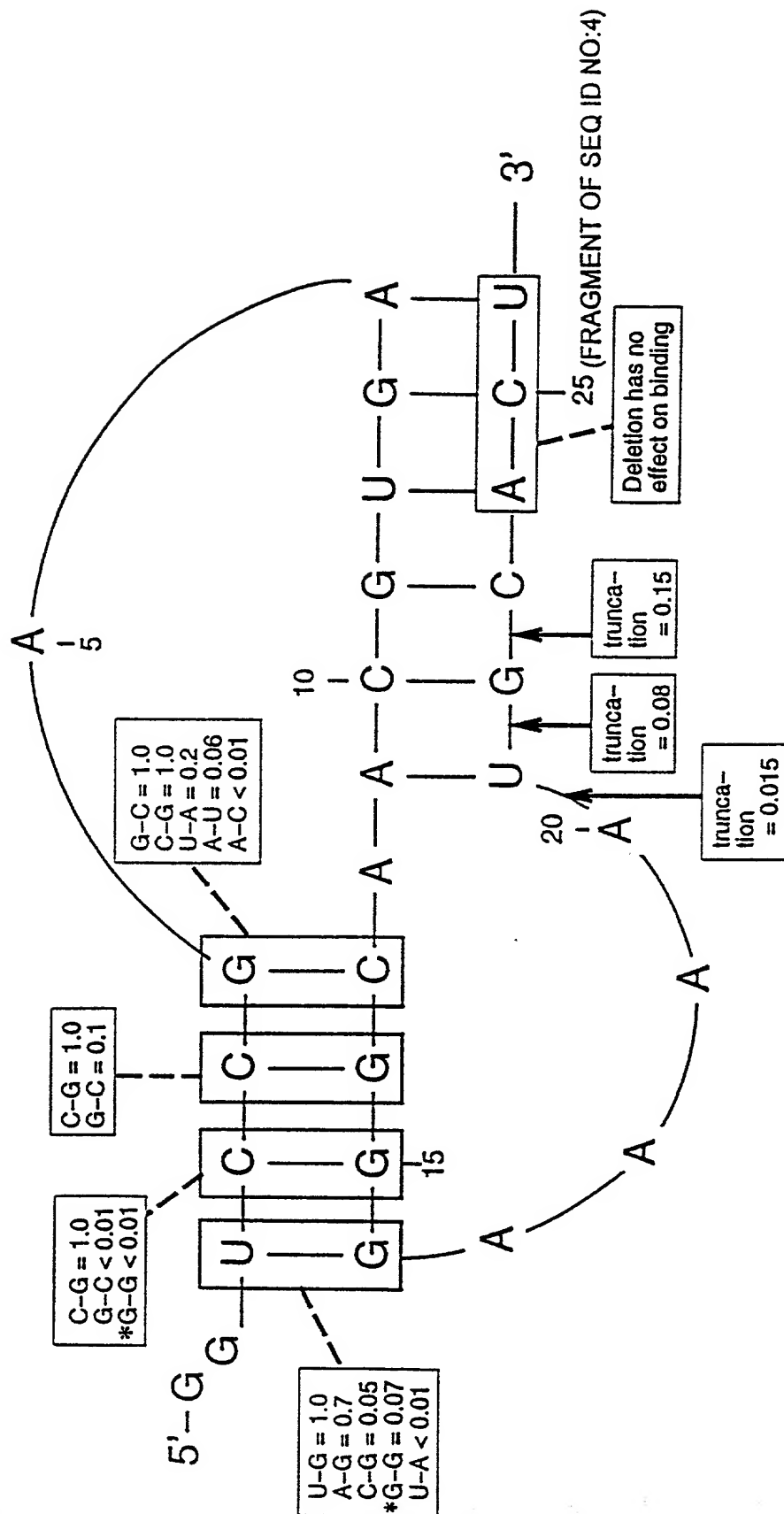


FIG. 3



FIG. 4

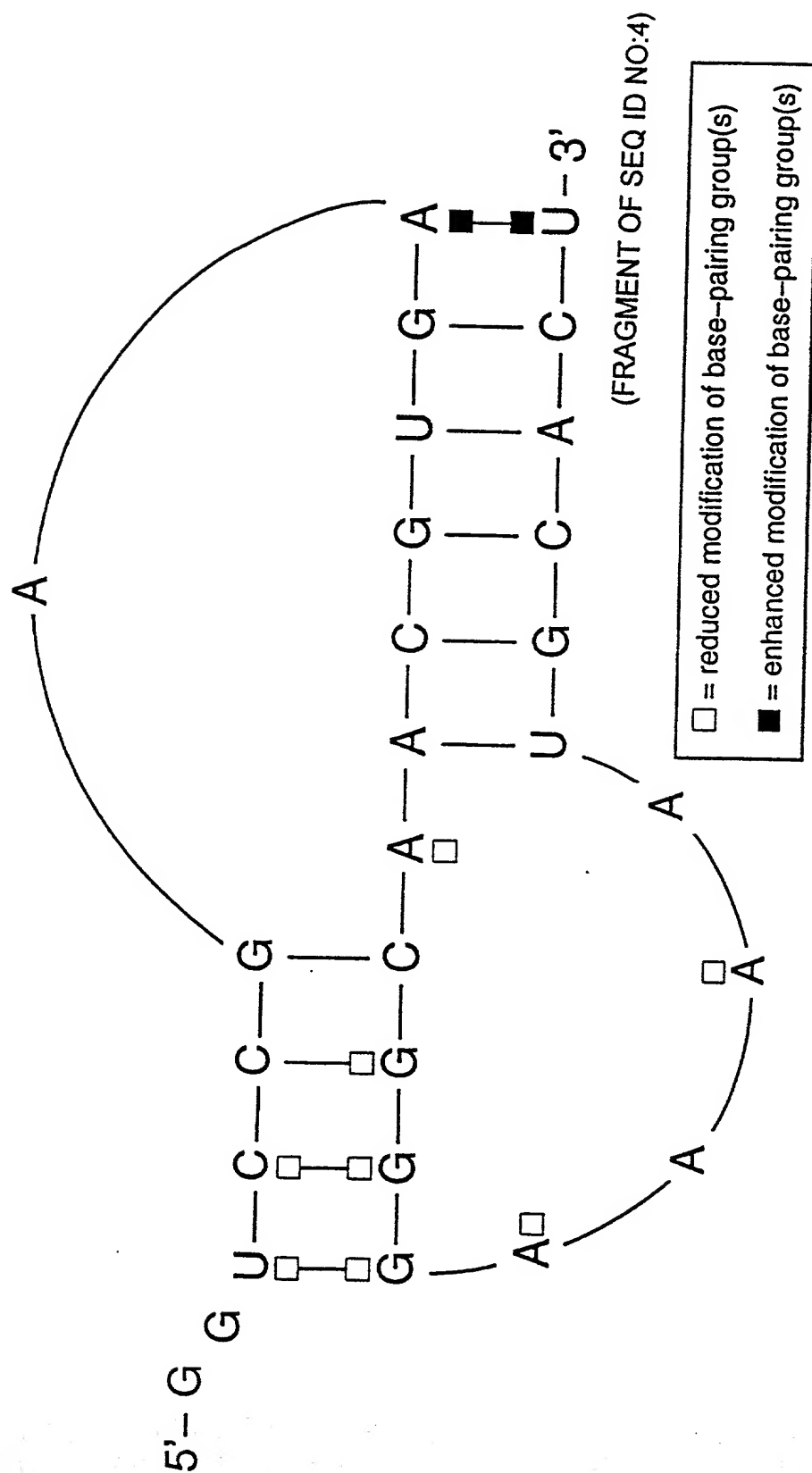


FIG. 5

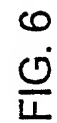
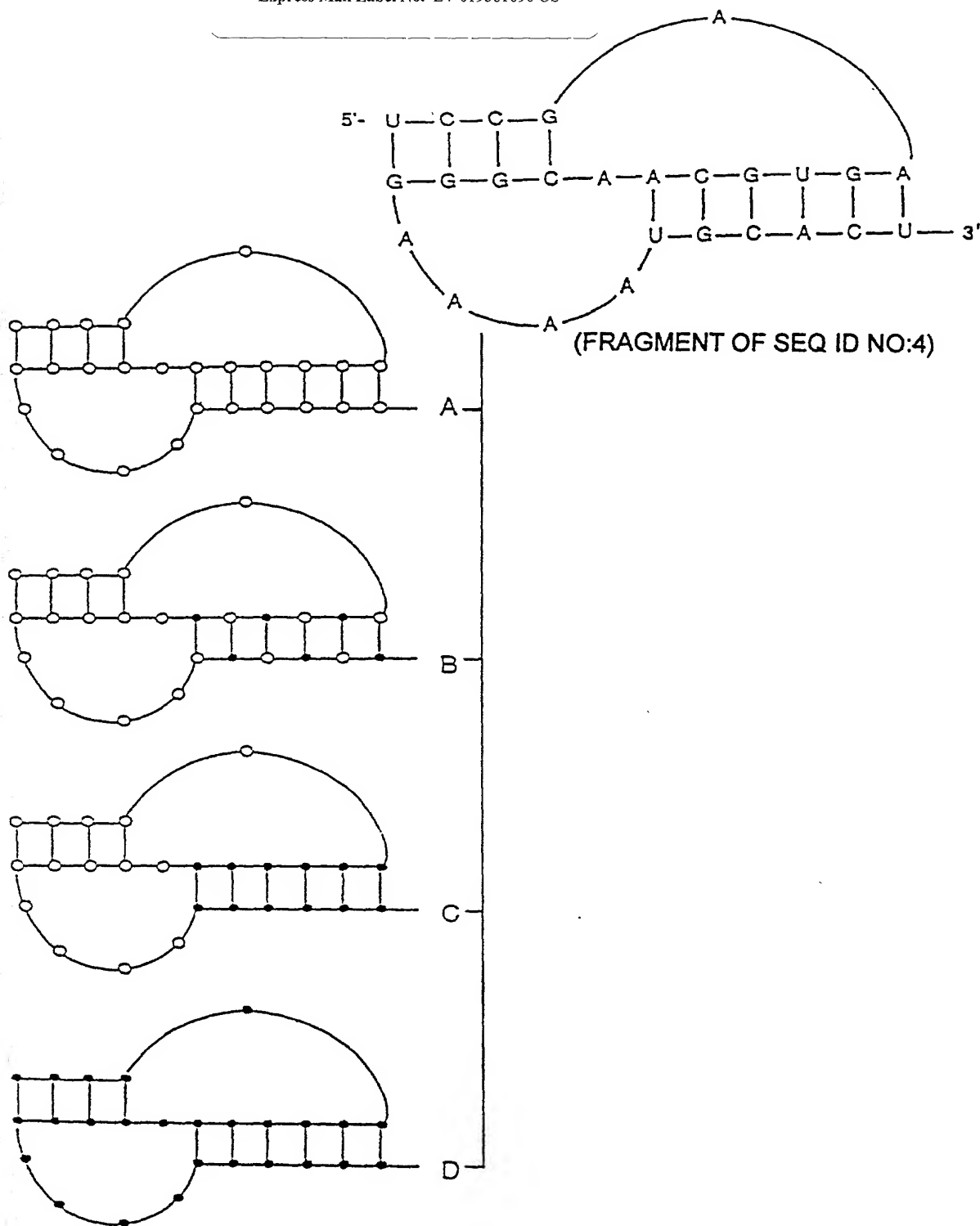


FIG. 6



● : denotes a 2' O-methyl instead of an OH,
denoted by (O), at this position on the ribose

FIG. 7A

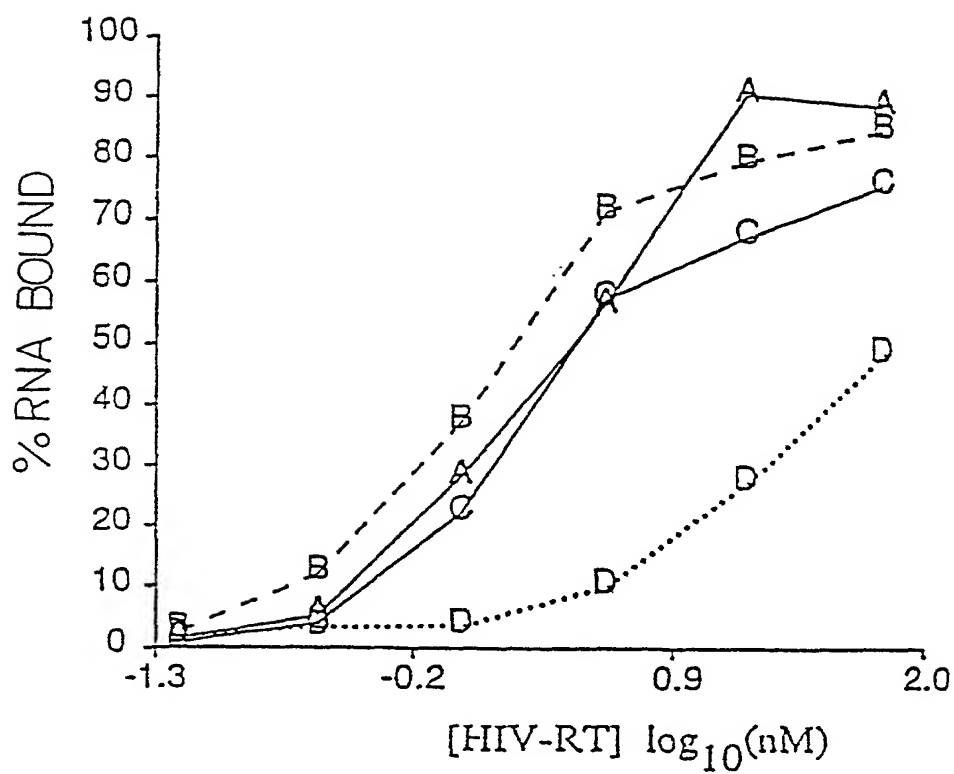


FIG.7B

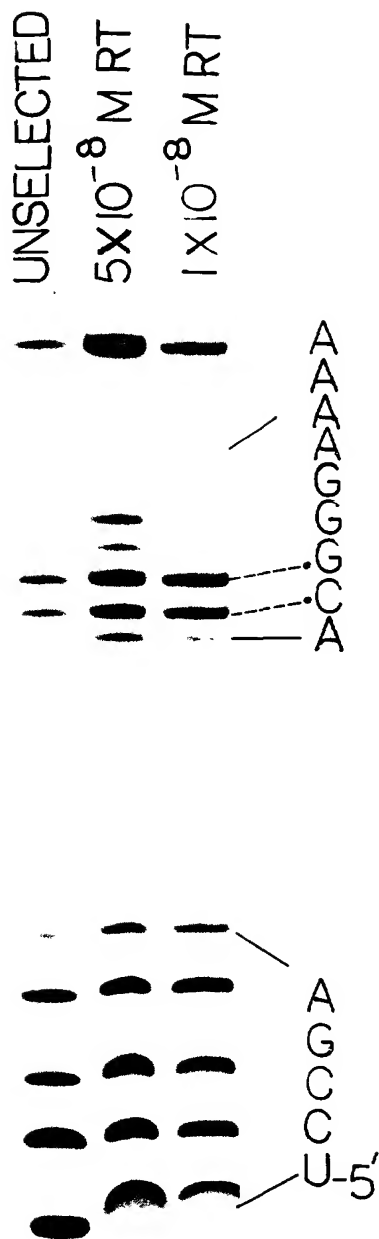


FIG. 8

5' -GGUCCGAAGUGCAACGGGAAAAUGCACU- [30N] -
CUAUGAAAGAAUUUUUAUAUCUCUAUUGAAAC-3'

SEQ ID NO.: 37

Isolate number

SEQ ID NO:

3, 22, 29	uAGCUC <u>UGAGG</u> CUUU—CGU <u>GUGUUC</u> QGAGcuau	14
14	uGCAU <u>UGAGG</u> CGGU—AA <u>GCGUUC</u> QGUGcu	15
20	uGGUGA <u>UGAGG</u> CCG—AU <u>GCGUUC</u> QUGCCGcu	16
4	uGACG <u>UGAGG</u> UCUU—GGU <u>ACUGUUC</u> QGUGGCcu	17
30	uCUGG <u>UGAGG</u> ACUUG—AA <u>GUGUUC</u> QCCAGGUcu	18
38	uCCCG <u>UGAGG</u> CAUA—AU <u>GCGUUC</u> QUGGGGUcu	19
39	uGGGA <u>UGAGG</u> UU—CC <u>CGUUC</u> QUGCCGCACCcu	20
2, 6, 9	uAGCGA <u>UGAGG</u> UA—UA <u>CUGGUC</u> QAUCGUGcu	21
13, 26	uCACAG <u>UGAGG</u> CUU—CU <u>GUGGUC</u> QUGUGUGcu	22
7	uUGU <u>UGAGG</u> UUGAUUCCA <u>UGGUC</u> QAACcu	23
35	uGCCU <u>UGAGG</u> CUGU—UU <u>AGCGGUC</u> QAGGUGCUcu	24
24	uCAAG <u>UGAGG</u> ACUU—AG <u>UCUGCUC</u> QUGUGcu	25

8	uUGCG <u>UGAGG</u> UUA—UU <u>CUGGUC</u> GAUGCCAcu	26
40	uUUCAG <u>UGAGG</u> UAUG—UAAUGA <u>UGGUC</u> GUGCGCcu	27

1	uGCGGAGAG <u>UGG</u> UU—UU <u>GACGUUG</u> CUCCUGCGcu	28
17	uCAUGGGAGCC <u>CAU</u> CGA—UUC <u>UGGGUGU</u> UGCcuaua	29
23, 27	uUGCACAGAGCC <u>AAA</u> —UUU <u>UGUGUUG</u> CUUGUGcu	30
18, 34	uGGCCAGAGCU <u>UAA</u> —UUC <u>AGUGUUG</u> CUGGCCcu	31
19	uCAUAGCAGUCC <u>UUG</u> AUACUAUG <u>GAUGGUGG</u> cuaua	32
37	uGGAUGCAAGU <u>UAA</u> —CU <u>CUGGUGG</u> CAUCCGUCcu	33

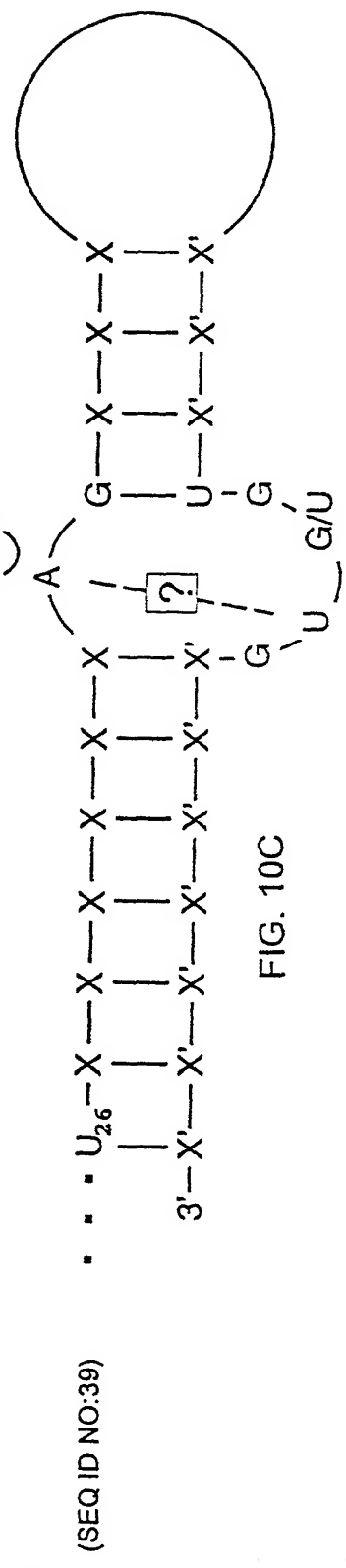
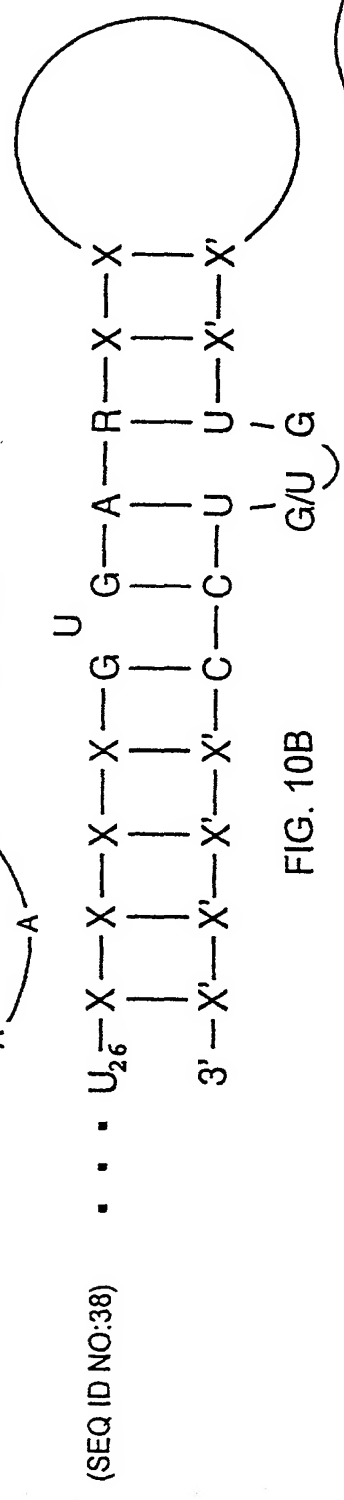
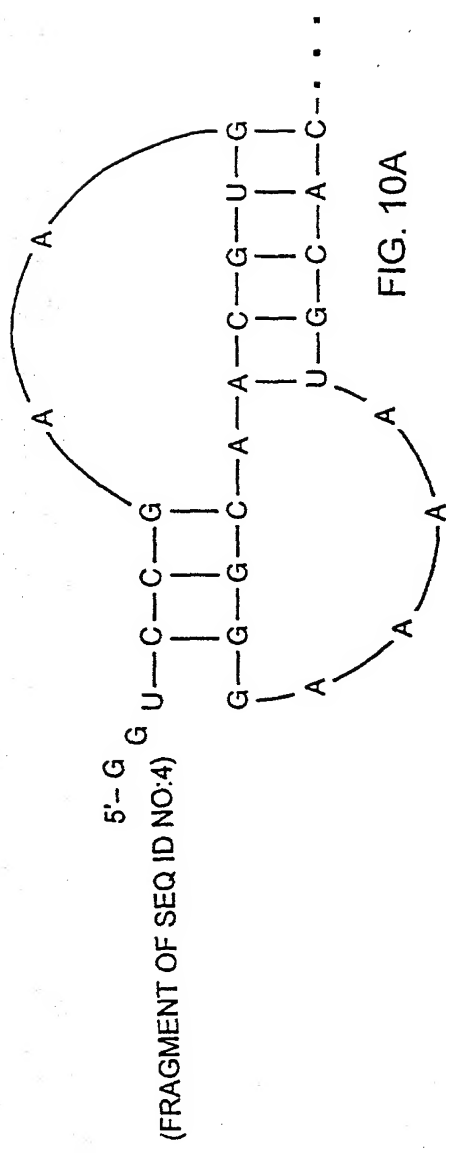
31 uCAGUGGAGAUUAAGCCUCGCUAGGGGCGCcuau

34

FIG. 9

20210101 1004049 010702

20200701 20200701



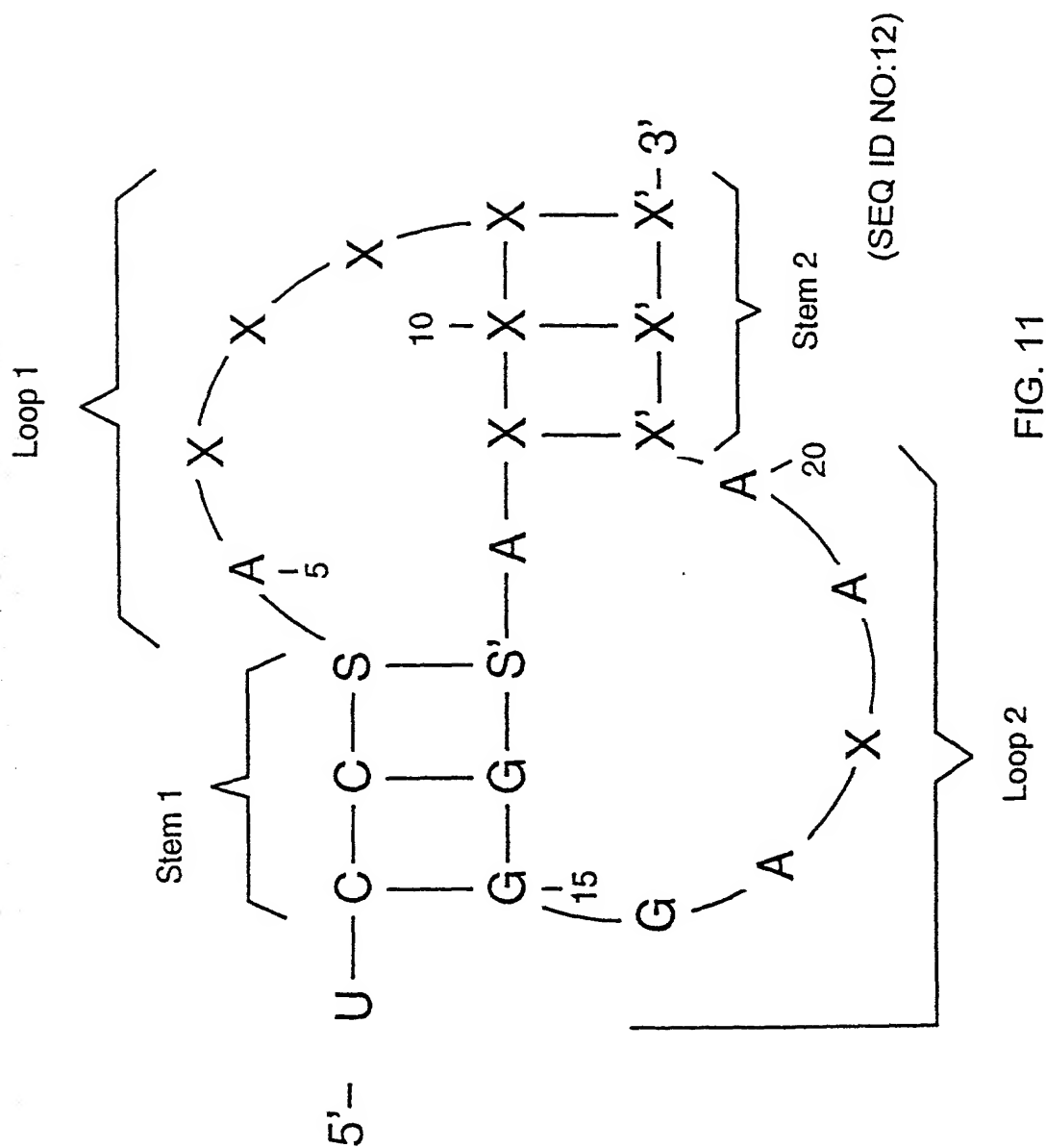


FIG. 11

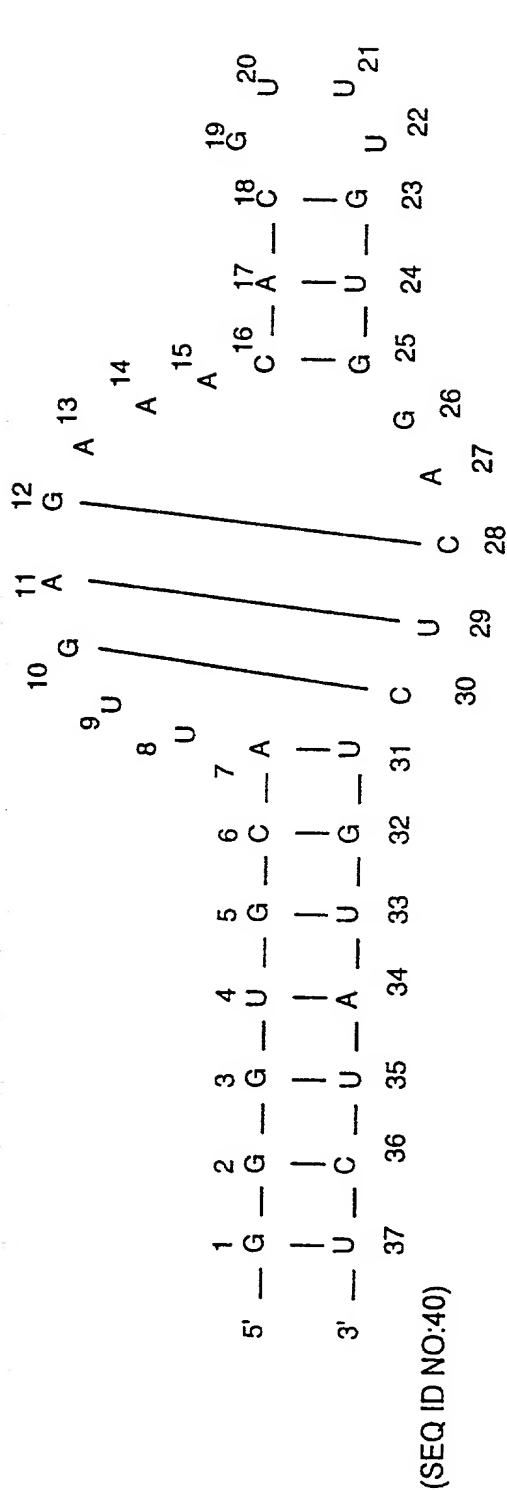


FIG. 12A

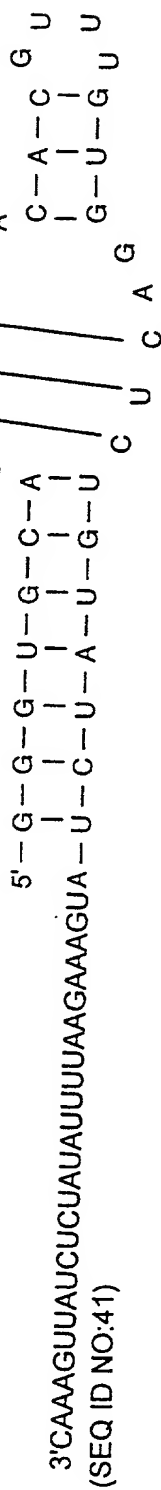


FIG. 12B

(SEQ ID NO:42) 5' GTTCAATAGAGATATAAAATTC 3'

FIG. 12C

modifying agent	partial		full
	less	more	
KETHOXAL	Δ	\triangleleft	\blacktriangle
DMS	\square	\boxtimes	\blacksquare
CMCT	\diamond	\diamondsuit	\blacklozenge
DEPC	\circ	\otimes	\bullet

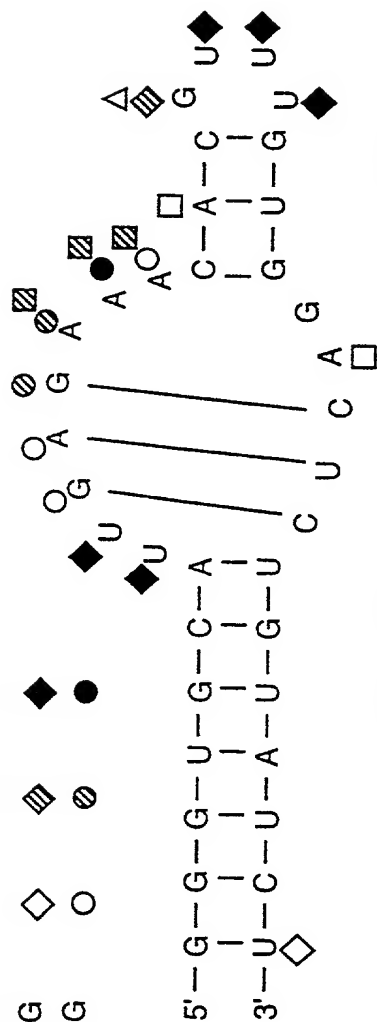
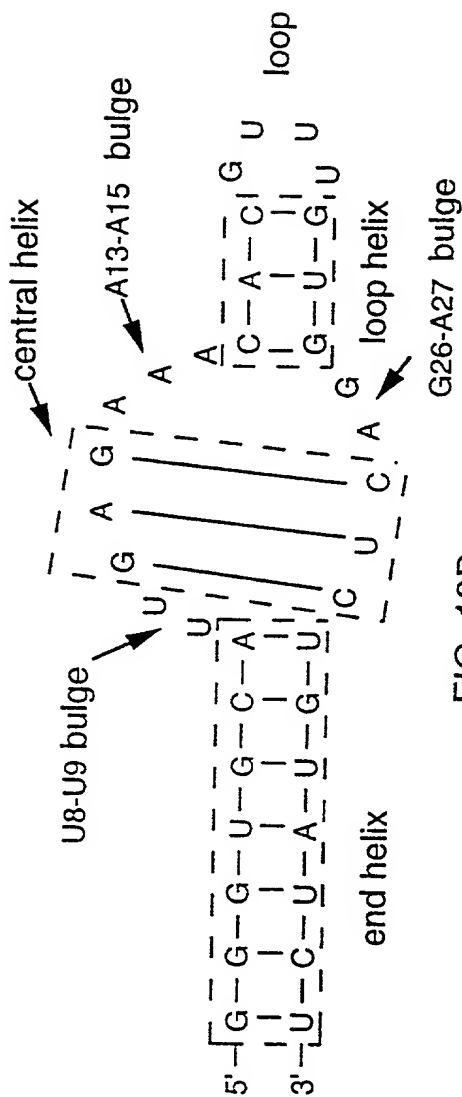
FIG. 13A
(SEQ ID NO:40)

FIG. 13B

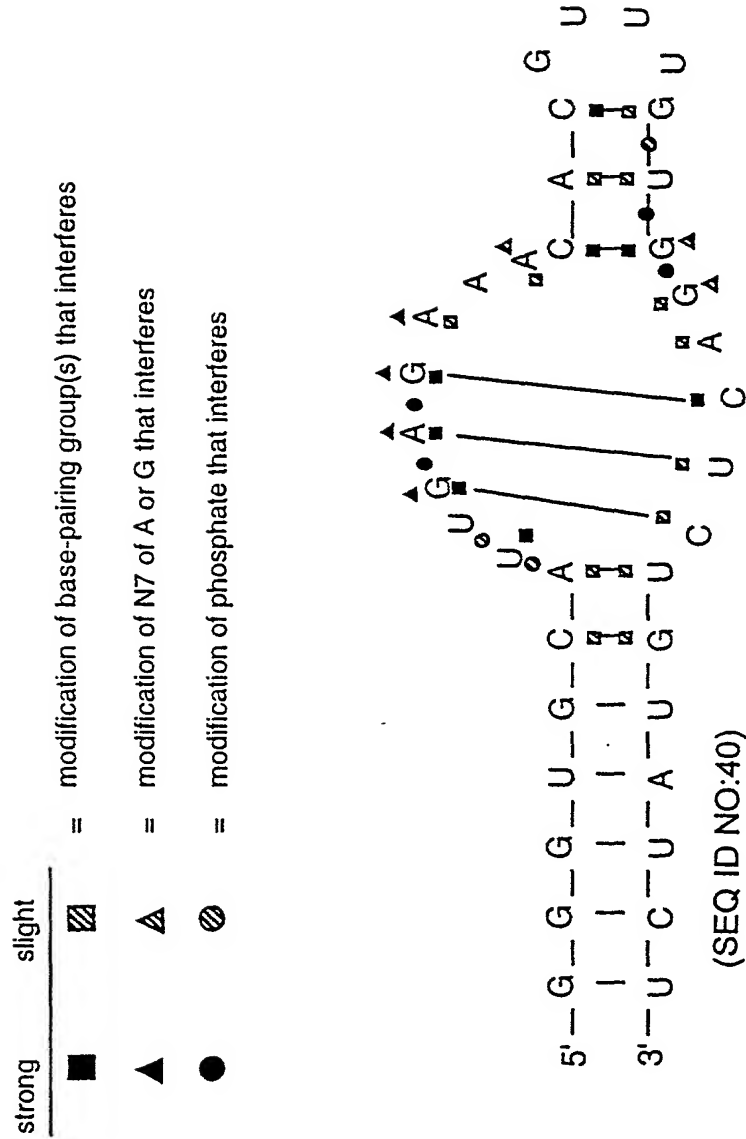


FIG. 14



FIG. 15



FIG. 16

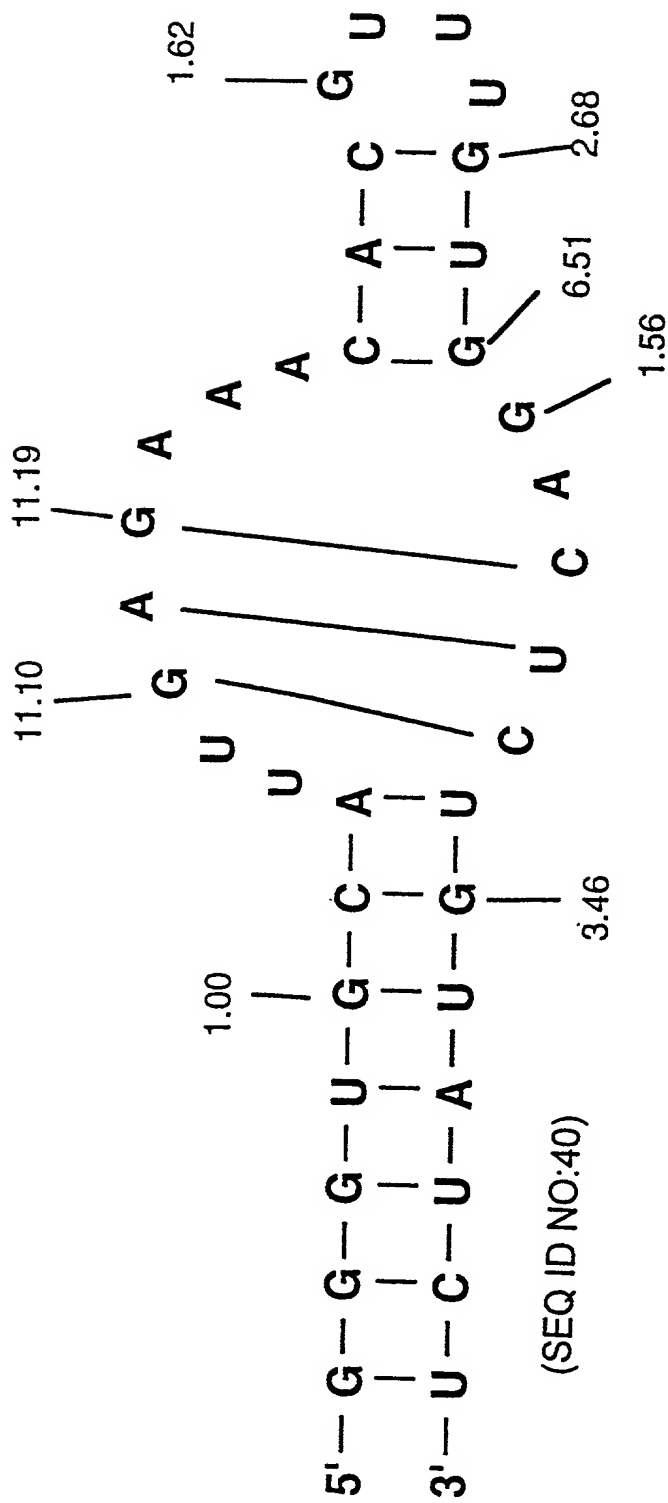


FIG. 17

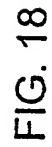




FIG. 19

▲ = enhanced modification of base



FIG. 20

SEQ ID NO.: 43

5' -GGGACUAUUGAUGGCCUCCGACC-6a-CACACAGAGUAAAGAGGAUCCGGG-3'

Biased ligand sequences

SEQ ID NO.:

6a GGGUGCAUUGAGAAACACGU-UUGUGACUCUGUAUCU 401 UGGUGCGUUGAGAAACAGGU-UUUUGGACUCUGUACCA 452 GUUUGCAUUGAGAGUCACAC-UUGUGGACUCUGCAUCC 463 AGAUGGAUUGAGAAACACUA-UUAUGGACUCUCCAUCC 474 AGCUUCGUGGAGAUACACGU-UGAUGGACUCCGAAGCA 485 UCGUACGUUGAGAAACAAAGU-UUAUGGACUCUGUAUCU 496 UCGAUCGUUGAGAUACACGC-UAGUGGACUCCGAAACU 508 UACUGCAUCGAGAUACACGU-UUGUGGACUCUGCACAU 519 UGAUACGUUGAGAAACACAA-UGCUGGACUCCGCAUCC 5210 GCCUGCAUUGAGAAACAGGA-UUCUGGACUCUGCCACU 5312 CGCUAUGUUGAGAAACACUU-UGCUGGACUCUGUAGCU 5413 UACUGCAUCGAGAAACACGU-AAGUG-ACUCUGCAUCC 5515 CGGUACGUGGAGAUACACGA-AGAUGGACUCUGUAVCG 56

FIG. 21-A

SEQ ID NO.:

17	<u>AA</u> <u>CU</u> <u>CC</u> <u>AU</u> <u>CG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CA</u> <u>CGA</u> - <u>UA</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>UG</u> <u>GAG</u> <u>CU</u>	57
18	<u>GG</u> <u>AG</u> <u>AC</u> <u>GU</u> <u>CG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CA</u> <u>CGU</u> - <u>UU</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>CG</u> <u>UC</u> <u>UCU</u>	58
21	<u>AG</u> <u>CU</u> <u>AC</u> <u>AU</u> <u>CG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>AGA</u> - <u>UU</u> <u>UG</u> <u>GA</u> <u>CUC</u> <u>UG</u> <u>UAG</u> <u>CG</u>	59
23	<u>AA</u> <u>GU</u> <u>GC</u> <u>AU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>AAU</u> - <u>GA</u> <u>UU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>UG</u> <u>CA</u> <u>cac</u>	60
24	<u>UG</u> <u>CU</u> <u>AC</u> <u>GU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CGU</u> - <u>UG</u> <u>AU</u> <u>GC</u> <u>AC</u> <u>UC</u> <u>CG</u> <u>UA</u> <u>AGCU</u>	61
25	<u>AG</u> <u>CU</u> <u>AC</u> <u>GU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CGU</u> <u>U</u> <u>AC</u> <u>GUG</u> - <u>CU</u> <u>CC</u> <u>GU</u> <u>AG</u> <u>CC</u>	62
27	<u>GAG</u> <u>UGG</u> <u>CUC</u> <u>GAG</u> <u>AA</u> <u>CA</u> <u>AGGU</u> - <u>UG</u> <u>CUG</u> <u>GAC</u> <u>UC</u> <u>GGC</u> <u>ACA</u> <u>U</u>	63
28	<u>UC</u> <u>GU</u> <u>GC</u> <u>GU</u> <u>CG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CGU</u> - <u>UG</u> <u>AU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>CGC</u> <u>ACA</u> <u>G</u>	64
29	<u>GG</u> <u>CA</u> <u>CC</u> <u>GU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CAU</u> - <u>GC</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>CG</u> <u>UG</u> <u>CCC</u>	65
30	<u>UCC</u> <u>UGCA</u> <u>UU</u> <u>GAG</u> <u>AA</u> <u>CA</u> <u>GUG</u> - <u>AU</u> <u>CUG</u> <u>GAC</u> <u>UC</u> <u>UGCA</u> <u>ACU</u>	66
31	<u>CU</u> <u>GU</u> <u>GG</u> <u>AU</u> <u>UG</u> <u>AG</u> <u>CA</u> <u>AC</u> <u>ACGU</u> - <u>GAG</u> <u>UGG</u> <u>AC</u> <u>UC</u> <u>UCC</u> <u>ACA</u> <u>U</u>	67
32	<u>CC</u> <u>GU</u> <u>GC</u> <u>GU</u> <u>UG</u> <u>AG</u> <u>AC</u> <u>AC</u> <u>CAC</u> - <u>CG</u> <u>AU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>CGC</u> <u>CAU</u> <u>GU</u>	68
33	<u>AG</u> <u>CU</u> <u>GC</u> <u>AU</u> <u>CG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CGA</u> - <u>UU</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>UGC</u> <u>AG</u> <u>CC</u>	69
35	<u>AGA</u> <u>UCC</u> <u>GU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CAU</u> - <u>GG</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>UCC</u> <u>CG</u> <u>CUA</u>	70
36	<u>AGA</u> <u>UGG</u> <u>AU</u> <u>UG</u> <u>AG</u> <u>AA</u> <u>CA</u> <u>CGU</u> - <u>UC</u> <u>GU</u> <u>GG</u> <u>AC</u> <u>UC</u> <u>UCC</u> <u>ACA</u> <u>U</u>	71
37	<u>GAC</u> <u>UGCA</u> <u>UC</u> <u>GAG</u> <u>AA</u> <u>CA</u> <u>CUG</u> - <u>AU</u> <u>GUG</u> <u>GGC</u> <u>UC</u> <u>CGC</u> <u>ACA</u> <u>CGG</u>	72

FIG. 21-B

SEQ ID NO.:

38	<u>AGCUACGUUGAGAAACA</u> <u>GUA</u> - <u>UAAUGGACUC</u> <u>CCGUAGCU</u>	73
40	<u>GAGUGCGUCGAGAAACA</u> <u>CAU</u> - <u>UUUGGACUC</u> <u>CCGCACAC</u>	74
42	<u>UCGUACGUUGAGAAACA</u> <u>CCG</u> - <u>UAGUGGACUC</u> <u>CCGUAGU</u>	75
43	<u>AGAUAACGUUGAGAGACA</u> <u>CCG</u> - <u>ACGUGGACUC</u> <u>CCGUAGUCU</u>	76
44	<u>AGGAUACACAGAGAAA</u> <u>CACCGUGGUGG</u> - <u>CUC</u> <u>CCUCUAU</u>	77
45	<u>GUGCGCAUCGAGAAA</u> <u>CACGU</u> - <u>UGAUGGACUC</u> <u>UGCAUGCAC</u>	78
47	<u>GAGAGGAUCGAGAAA</u> <u>CACGU</u> - <u>AUGUGGACUC</u> <u>UCCAUUCU</u>	79
48	<u>GGAUGGAUUGAGACA</u> <u>CACGU</u> - <u>AUGUGGACUC</u> <u>UCCAUCA</u>	80
49	<u>UCGGGCAUUGAGAU</u> <u>CACGU</u> - <u>AGAUGGACUC</u> <u>UGUCUCA</u>	81
50	<u>UGGACCGUAAGAGAAA</u> <u>CACGUUUGAUGG</u> - <u>CUC</u> <u>CCUCUGU</u>	82

FIG. 21-C

6a	G	G	G	U	G	C	A	U	U	G	A	G	A	A	A	C	A	C
wt	10	19	16	30	20	31	18	37	22	38	38	38	36	25	38	38	38	30
A	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A	12	8	8	5	11	0	18	0	2	0	38	0	36	25	38	0	38	3
C	3	8	14	1	3	31	1	1	14	0	0	0	2	2	0	38	0	30
G	10	19	16	2	20	4	19	0	0	38	0	38	0	2	0	0	0	5
U	19	2	0	30	4	1	0	37	22	0	0	0	0	9	0	0	0	0
bp	16	20	26	31	33	35	35			38	38	38				38	38	26

FIG. 22A-1

6a	G	G	G	U	G	C	A	U	U	G	A	G	A	A	A	C	A	C
wt	.26	.50	.42	.79	.53	.82	.47	.97	.58	1.00	1.00	1.00	.95	.66	1.00	1.00	1.00	.79
D	.00	.03	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
A	.32	.21	.21	.13	.29	.00	.47	.00	.05	.00	1.00	.00	.95	.66	1.00	.00	1.00	.08
C	.08	.21	.37	.03	.08	.82	.03	.03	.37	.00	.00	.00	.05	.05	.00	1.00	.00	.79
G	.26	.50	.42	.05	.53	.11	.50	.00	.00	1.00	.00	1.00	.00	.05	.00	.00	.00	.13
U	.50	.05	.00	.79	.11	.03	.00	.97	.58	.00	.00	.00	.00	.24	.00	.00	.00	.00
bp	.42	.53	.68	.82	.87	.92	.92	.00	.00	1.00	1.00	1.00	.00	.00	.00	1.00	1.00	.68

FIG. 22B-1

202070" 2640400T

G	U	space	U	U	G	U	G	G	A	C	U	C	U	G	U	A	U	C	U
25	22	35	23	14	19	38	38	37	36	38	38	38	15	28	17	31	15	26	19
0	0	35	0	0	0	0	0	1	3	0	0	0	0	0	0	0	0	0	0
7	8	0	9	7	11	0	0	0	36	0	0	0	2	0	0	31	4	7	3
1	5	0	1	4	5	0	0	0	0	38	0	38	20	9	20	6	10	26	11
25	3	0	5	13	19	0	38	37	0	0	0	0	1	28	1	1	9	5	5
5	22	3	23	14	3	38	0	0	0	0	38	0	15	0	17	0	15	0	19
18				18	26	38	38			38	38	38	33	35	35	31	26	20	16

FIG. 22A-2

G	U	space	U	U	G	U	G	G	A	C	U	C	U	G	U	A	U	C	U
.66	.58	.92	.61	.37	.50	1.00	1.00	.97	.95	1.00	1.00	1.00	.45	.74	.39	.82	.39	.68	.50
.00	.00	.92	.00	.00	.00	.00	.00	.03	.08	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
.18	.21	.00	.24	.18	.29	.00	.00	.00	.95	.00	.00	.00	.00	.00	.05	.82	.11	.18	.08
.03	.13	.00	.03	.11	.13	.00	.00	.00	.00	1.00	.00	1.00	.53	.24	.53	.16	.26	.68	.29
.66	.08	.00	.13	.34	.50	.00	1.00	.97	.00	.00	.00	.00	.03	.74	.03	.03	.24	.13	.13
.13	.58	.08	.61	.37	.08	1.00	.00	.00	.00	.00	1.00	.00	.45	.00	.39	.00	.39	.00	.50
.47	.00	.00	.00	.47	.68	1.00	1.00	.00	.00	1.00	1.00	1.00	.92	.92	.87	.82	.68	.53	.42

FIG. 22B-2

6a	G	G	G	U	G	U	G	C	A	U	G	A	G	A	A	C	A	C
wt	-.37	-.13	-.21	.16	-.10	.19	-.16	.34	-.05	.37	.37	.32	.03	.37	.37	.37	.37	.16
A	.19	.09	.09	.01	.16	-.13	-.16	-.13	-.07	-.13	.37	.32	.03	.37	.37	-.13	.37	-.05
C	-.05	.09	.24	-.09	-.05	.19	-.10	-.10	.24	-.13	.37	-.07	-.07	-.13	.37	.37	-.13	.16
G	-.37	-.13	-.21	-.07	-.10	-.02	.38	-.13	-.13	.37	-.13	-.13	-.07	-.13	-.13	-.13	-.13	.01
U	.38	-.07	-.13	.16	-.02	-.10	-.13	.34	-.05	-.13	-.13	-.13	.11	-.13	-.13	-.13	-.13	-.13

FIG. 22C-1



20240707 2640400F

G	U	space	U	U	G	U	G	G	A	C	U	C	U	G	U	A	U	C	U
.03	-.05		-.02	-.26	-.13	.37	.37	.34	.32	.37	.37	.37	.11	-.18	-.24	.19	-.24	.05	-.13
.06	.09		.11	.06	.16	-.13	-.13	-.13	.32	-.13	-.13	-.13	-.13	-.13	-.07	.19	-.02	.06	-.05
-.10	.01		-.10	-.02	.01	-.13	-.13	-.13	-.13	.37	-.13	.37	.11	.40	.40	.03	.14	.05	.16
.03	-.05		.01	.22	-.13	-.13	.37	.34	-.13	-.13	-.13	-.13	.11	-.10	-.10	-.10	.11	.01	.01
.01	-.05		-.02	.26	-.05	.37	-.13	-.13	-.13	-.13	.37	-.13	-.13	.11	-.24	-.13	-.24	-.13	-.13



FIG. 22C-2

20201026404001

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	2	16	8	28	2	28	16	38	38	19	9
AU	6	0	6	0	10	0	16	0	38	0	2
UA	2	1	0	28	2	0	0	0	0	2	1
GC	5	16	7	2	18	6	18	0	0	3	3
CG	1	2	8	0	1	28	1	38	0	19	1
GJ	1	1	8	0	2	0	1	0	0	1	9
UG	4	1	0	0	0	1	0	0	0	0	0
AC	3	3	0	2	1	0	2	0	0	0	1
CA	1	1	2	0	0	0	0	0	0	9	0
other	16	13	7	8	2	3	0	0	0	4	14

FIG. 23A

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	.05	.42	.21	.74	.05	.74	.42	1.00	1.00	.50	.24
AU	.16	.00	.16	.00	.26	.00	.42	.00	1.00	.00	.05
UA	.05	.03	.00	.74	.05	.00	.00	.00	.00	.05	.03
GC	.13	.42	.18	.05	.47	.16	.47	.00	.00	.08	.08
CG	.03	.05	.21	.00	.03	.74	.03	1.00	.00	.50	.03
GJ	.03	.03	.21	.00	.05	.00	.03	.00	.00	.03	.24
UG	.11	.03	.00	.00	.00	.03	.00	.00	.00	.00	.00
AC	.08	.08	.00	.05	.03	.00	.05	.00	.00	.00	.03
CA	.03	.03	.05	.00	.00	.00	.00	.00	.00	.24	.00
other	.42	.34	.18	.21	.05	.08	.00	.00	.00	.11	.37

FIG. 23B

6a	G1/U37	G2/C36	G3/U35	U4/A34	G5/U33	C6/G32	A7/U31	C16/G25	A17/U24	C18/G23	G19/U22
WT	-.34	.03	-.18	.35	-.34	.35	.03	.61	.61	.11	-.15
AU	.08	-.02	.08	-.02	.19	-.02	.03	-.02	.61	-.02	-.03
UA	.04	.01	-.02	.35	.04	-.02	-.02	-.02	-.02	.04	.01
GC	.05	.03	.11	.04	.40	.14	.46	-.02	-.02	.06	.00
CG	.01	.04	.19	-.02	.01	.35	.01	.61	-.02	.11	.01
CJ	-.34	-.05	-.18	-.02	-.34	-.02	-.05	-.02	-.08	.01	-.15
UG	.09	.01	-.02	-.08	-.02	-.05	-.02	-.08	-.02	-.08	-.02
AC	.06	.00	-.02	.04	.01	-.02	-.03	-.02	-.08	-.02	.01
CA	.01	.01	.04	-.08	-.02	-.08	-.02	-.08	-.02	.16	-.02
other	.17	.09	-.07	-.04	-.20	-.17	-.25	-.25	-.25	-.15	.12

FIG. 23C

204070" 2640400T

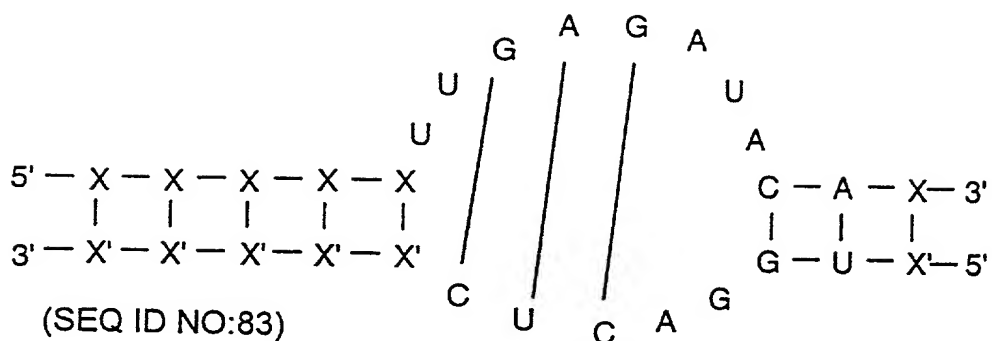


FIG. 24A

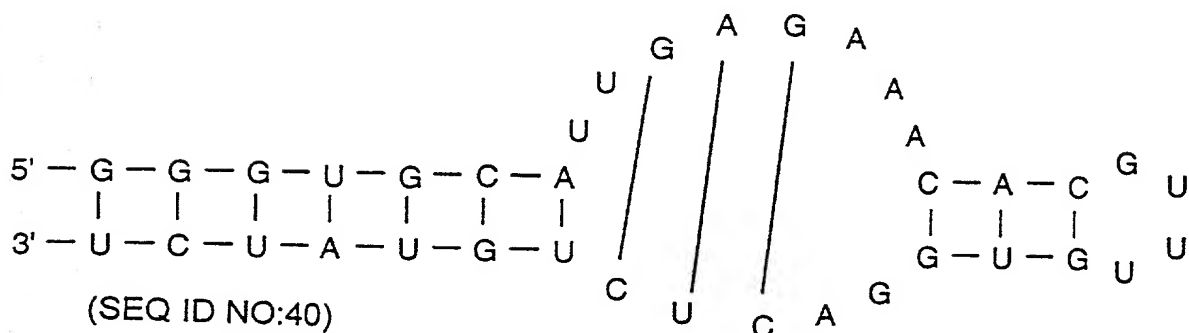


FIG. 24B

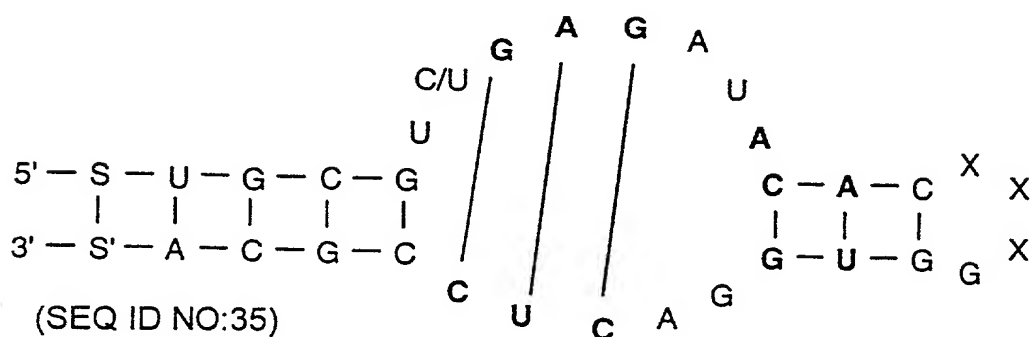


FIG. 24C

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